REMARKS

I. Status of the Claims

Claims 41, 43-48, 55-57, and 59-62 were pending at the time the Office Action dated February 3, 2010 ("the Action"), was mailed. No claims are amended, canceled, or newly added. Claims 41, 43-48, 55-57, and 59-62 remain pending.

II. The Obviousness Rejection of Claims 41, 43-48, 55-57, and 59-62 Is Overcome

The previous obviousness rejection was based on a combination of Arita (*Biochem. Biophys. Res. Comm. 257*:79 (1999)), Kondo (*Diabetes 51*:2325 (July 2002)), Ellsworth (U.S. Patent No. 6,414,126), Weyer (*J. Clin. Endocrin. Metabolism 86*:1930 (2005)), and Orsi (*Pharmacotherapy 21*:767 (2001)). In the present Action, the Examiner has withdrawn the Arita reference but maintains that the remaining art still establishes the obviousness of the claims. Thus, Claims 41, 43-48, 55-57, and 59-62 are rejected as unpatentable under Section 103(a) over a combination of Kondo, Ellsworth, Weyer, and Orsi.

Following a summary of the rejection, applicants demonstrate that the claims are patentable. In particular, applicants discuss Kondo, which shows that administration of hypolipidemic agents (also called antihyperlipidemic agents in this reference) does not necessarily result in increased adiponectin levels. This fact challenges the Examiner's rationale behind the rejection such that the rejection is improper.

1. Summary of the Rejection

Applicants provide the following summary of the rejection. Should any aspect of the summary be incorrect or inaccurate, applicants respectfully request clarification by the Examiner.

The Examiner relies on Kondo as the primary reference in the rejection. Kondo describes type 2 diabetes-suffering test subjects in the context of a study designed to examine adiponectin

gene mutations. Kondo, Abstract. Some of these subjects were taking hypolipidemic agents to treat lipid abnormalities (*id.* at page 2326, second full paragraph; see also Table 2, referring to antihyperlipidemic agents), which is noted by the Examiner at page 8 of the Action. The Examiner appears to conclude that Kondo teaches that "lipid abnormalities such as hypoadiponectinemia can be treated with hypolipidemic agents." Action, page 3.

Turning to Ellsworth, this reference teaches that a combination of a C-aryl glucoside and a lipid lowering agent, such as an HMG-CoA reductase inhibitor, may be employed to treat certain conditions, such as hyperlipidemia and diabetes. Ellsworth, Col. 1, lines 10-16; and Col. 31, lines 27-30. Several statins, including pravastatin and rosuvastatin, are listed as examples of such inhibitors. See *id.* at Col. 31-32 and Claim 23. Because the present claims recite methods *comprising* administration of an HMG-CoA reductase inhibitor, the Examiner continues to assert that Ellsworth's teachings are relevant.

Weyer is cited as teaching that conditions such as obesity and type 2 diabetes are associated with low adiponectin levels in patients. Weyer, Abstract. Orsi is once again relied upon for a teaching that a skilled artisan would be prompted to utilize water-soluble HMG-CoA reductase inhibitors due to their lower toxicity profiles. Action, page 4.

The Examiner takes the teachings of these references to conclude that it was expected that administration of an HMG-CoA reductase inhibitor would necessarily result in the increase of adiponectin levels and the treatment of hypoadiponectinemia:

> At any given time during the administration of one or more HMG CoA-reductase inhibitors to the subject of claim 1, the increase of adiponectin ***will occur***.

Action, page 12; and

> The one of skill would readily recognize that with the administration of one or more water-soluble HMG-CoA reductase inhibitors for metabolic diseases and disorders for which they are readily indicated, that in the process of treatment adiponectin ***would be affected***.

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Id. at page 14 (emphases added).

The Examiner makes no mention, in this Action or the previous Action, of applicants' showing that there was no reasonable expectation of success that administration of an HMG-CoA reductase inhibitor would increase adiponectin production or that administration of a water soluble HMG-CoA reductase inhibitor would treat hypoadiponectinemia as claimed.

2. The Rejection is Factually Unsupported

Although Arita has been removed from the list of references relied upon by the Examiner, applicants' comments in the Response filed July 29, 2009, are repeated and incorporated herein, including comments regarding applicants' evidence demonstrating that any assertion that an HMG-CoA reductase inhibitor would obviously and definitively "increase" or "affect" adiponectin production is unfounded and cannot support an obviousness rejection. In addition to these comments, the following additional factual evidence counters the Examiner's conclusions regarding the cited art. Data associated with Kondo's test subjects, in particular, demonstrates that the Examiner has failed to factually support a prima facie case of obviousness as required by M.P.E.P. § 2142 ("The examiner bears the initial burden of factually supporting any *prima facie* case of obviousness.").

Applicants first note that the Specification indicates that HMG-CoA reductase inhibitors are hyperlipemia (hyperlipidemia) therapeutic medicaments (page 5, lines 30-32, of the English translation) and can therefore be considered antihyperlipidemic drugs. Table 2 of Kondo describes the clinical profile of test subjects examined therein and indicates that five of the subjects were on an antihyperlipidemic drug when the study commenced. Looking at the adiponectin levels of these five subjects compared to subjects who were not taking any such agent, one cannot conclude that administration of such an agent increased adiponectin levels. For example, Test Subject #6, who was taking an antihyperlipidemic drug, had a lower

adiponectin level (1.8 μg/ml) than Test Subject #4 (2.6 μg/ml), who was not taking such a drug. This information directly challenges the Examiner's conclusions regarding the effects of antihyperlipidemic drugs on adiponectin levels, such as recited on pages 13-14 of the Action. In other words, Kondo's test subject data disproves the Examiner's contention that taking an antihyperlipidemic drug, such as an HMG-CoA reductase inhibitor, will necessarily result in increased adiponectin levels. Any combination of Kondo, Ellsworth, Weyer, and/or Orsi cannot ignore this fact.

In view of the above, there is no factual basis for the assertion that methods for increasing adiponectin production or treating hypoadiponectinemia using an HMG-CoA reductase inhibitor or water-soluble HMG-CoA reductase inhibitor, as presently claimed, are obvious. Applicants therefore respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe that Claims 41, 43-48, 55-57, and 59-62 are in condition for allowance. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicants' attorney at 206.695.1649.

Respectfully submitted,

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